reduced the occurrence of VAs (2.7±0.48, 2.5±0.53, 1.7±0.48 versus 3.3±0.95) and ameliorated the shortening of 90% repolarization of action potential durations (APD_{90}) and the dispersion of APD (APDd) during myocardial ischemia reperfusion.
Conclusions: Taxol pre-treatment reduces ischemia-related VAs, improved APD_{90}, preserves normal Cx43 expression and locations during myocardial ischemia. These findings provide potential therapeutic targets for ameliorating VAs during IR.

GW25-e0440

DPP-4 Inhibitors Repress Foam Cell Formation by Inhibiting Scavenger Receptors through Protein Kinase C Pathway

Dai Yao[1,2], Dai Dongsheng[3], Mehta Jawahar L[1]
[1]Department of Cardiology, University of Arkansas for Medical Sciences and the Central Arkansas Veterans Healthcare System, Little Rock, AR, [2]Department of Internal Medicine, The First Affiliated Hospital of Anhui Medical University, Hefei, Anhui, People's Republic of China, [3]Department of Cardiology, The First Affiliated Hospital of Anhui Medical University, Hefei, Anhui, People's Republic of China

Objectives: studies show that dipeptidyl peptidase-4 (DPP-4) inhibitors may have an anti-atherosclerotic effect. Since foam cells are key components of atherosclerotic plaque, we studied the effect of DPP-4 inhibitors on foam cell formation.
Methods: Foam cell formation was studied by treatment of primary and THP-1 macrophages with oxidized low density lipoprotein (ox-LDL) in the absence or presence of DPP-4 inhibitors (sitagliptin and NVPDPP728). The expression of scavenger receptors (SR) SRA, CD36 and LOX-1 was measured, and their role in foam cell formation in the presence of DPP-4 inhibitors was examined by their over-expression. In additional studies, role of protein kinase (PK) C and A in the effect of DPP-4 inhibitors was examined.
Results: Foam cell formation was markedly reduced by both DPP-4 inhibitors, as was the expression of CD36 and LOX-1 (CD36>>LOX-1), but not SRA. Simultaneously, there was a reduction in phosphorylated-PKC, but not PKA, content. Recovery of phosphorylated-PKC following treatment of cells with PMA negated the effect of DPP-4 inhibitors on foam cell formation. Further, over-expression of CD36 or LOX-1 blocked the effect of DPP-4 inhibitors on foam cell formation.
Conclusions: DPP-4 inhibitor exerts a potent inhibitory effect on foam cell formation from human macrophage cell line in response to ox-LDL. This effect is primarily mediated by decrease in the expression of two different SRs on monocytes/macrophages CD36 and LOX-1. This results in a decrease in ox-LDL internalization. DPP-4 inhibitors also exert a potent inhibitor effect on PKC activation, perhaps mediated by membrane-bound DPP-4, which plays a critical role in foam cell formation, inflammation and atherogenesis.

GW25-e0502

Association of SOCS3 genetic polymorphisms with insulin resistance in Xinjiang Uygur population

Jingjing Zhang, Nanfang Li, Yao Xiao-Guang, Zhou Ling, Zhang Ju-Hong, Lin Na, Hong Jing
Hypertension center of People's Hospital of Xinjiang

Objectives: To investigate the association between suppressor of cytokine signaling 3 (SOCS3) genetic polymorphisms and insulin resistance (IR) in Xinjiang Uygur population.
Methods: In this cross-sectional study on the metabolic diseases (e.g. obesity) among Uygur Chinese in Hetian, Xinjiang China,1292 Uygur individuals were enrolled. The sample size for IR subjects [homeostasis model assessment for insulin resistance (HOMA-IR) ≥2.96] was 323, whereas that for non-IR controls was 969 (HOMA-IR<2.96). Representative variations were selected according to gene database and genotyping using the TaqMan polymerase chain reaction method in 1292 Uygur individuals. A relatively isolated general population in a relatively homogeneous environment and a case-control study was conducted to test the association between the genetic variations of SOCS3 gene and insulin resistance.
Results: There was significant difference of genotype distribution of rs4969168 between insulin resistance and control groups in the male population (P=0.027). Although the insulin resistance related quantitative phenotypes have no significantly difference in individuals with GG AG and AA genotypes of rs4969168 in total, male and female population (P>0.05) the mean of body mass index and the median of fasting insulin increased in individuals with GG AG AA genotypes of rs4969168 in male population. But not in total and female population. Haplotype 2 (rs12953258C-rs4969168A-rs9914220C) was significantly associated with a higher prevalence of IR in male population (P=0.023). The logistic regression analysis showed that AG genotype of rs4969168 variation might be a protective factor for insulin resistance in male (OR=0.564, 95% confidence interval 0.344-0.925. P=0.023).
Conclusions: The present study suggests that the rs4969168 polymorphism in SOCS3 gene may be associated with insulin resistance in Xinjiang Uygur men.

GW25-e0520

Cardioprotective effect of sCR1 on myocardial ischemia-reperfusion injury in Rats

Guo Wenyun, Huang Lan
Institute of Cardiovascular Diseases of PLA, Xinqiao Hospital, Third Military Medical University, Chongqing, People's Republic of China

Objectives: The aim of this study was to investigate the effects of soluble complement receptor 1 (sCR1) on rat models of myocardial I/R, explore its potential mechanisms of cardioprotection.
Methods: Myocardial ischemia-reperfusion model was built, randomly assigned to sham operation group (SOG) and ischemia reperfusion group (IRG) and sCR1 pre-treatment group (CPG). Observation on myocardial infarct size and microstructure of each group, using RT-PCR and Elisa to detect expression of LC3-II and Beclin1 mRNA and protein.
Results: Compared with IRG, myocardial infarct size and microstructure damage are reduced in CPG. The mRNA and protein of Beclin1 and LC3-II were detected in each group of Myocardial, while in CPG increased than IRG.
Conclusions: sCR1 could protect myocardial ischemia-reperfusion injury, may be associated with fading excessive autophagy in myocardiac.

GW25-e0544

Effects of Salvianolic acid on proliferation, adhesion and NO secretion activity of human peripheral endothelial progenitor cells

Yan Feng-Di, He Shenghu
Department of Cardiology, Northern Jiangsu People's Hospital, Affiliated Hospital to Yangzhou University, Yangzhou, 225001, China

Objectives: To investigate the effects of salvianolic acid on the proliferation, adhesion and nitric oxide (NO) secretion activity of endothelial progenitor cells (EPCs) cultured in vitro.
Methods: The mononuclear cells (MNCs) were isolated from human peripheral blood by Ficoll density gradient centrifugation, and then the cells were planted on the human fibronectin (FN) coated culture dishes. The cells were suspended in endothelial basal medium (EBM-2) supplemented with EGM-2-MV-SingleQuots. EPCs were characterized as adherent cells double positive for DiL-acLDL uptake and lectin binding by direct fluorescent staining under a laser scanning confocal microscope. After cultered for 7 days, EPCs were randomized into 6 groups: control group, simvastatin group and different concentrations of salvianolic acid groups (0.5, 2.5, 5,10mg/L). After different periods of culturing (24h,48h,72h) the ability of cell proliferation was assayed with MTT assay, counting adherent cells assayed the adhesion activity of EPCs, the NO content was measured in the cell culture medium by nitrate reductase method to find the effect on cell secretion activity.
Results: Incubation of EPCs with Salvianolic acid increased the number of EPCs, with a maximum at 5mg/L after 24 hours (P<0.01). In addition, Salvianolic acid promotes EPCs proliferative, adhesive and NO secreting capacity.
Conclusions: Salvianolic acid can promote EPCs augmentation and enhance its proliferation, adhension and NO secreting function. It is likely to be a new mechanism of EPCs for therapy ischemic disease.

GW25-e0549

RNA interference targeting E637K mutation rescues hERG channel currents and restores its kinetic properties

Lu Xiaoli[1], Huang Chen[3], Sun Huanhuan[4], Lian Jiangfang[2]
[1]People's Hospital of Anji County, HuZhou, China, [2]LiHuiLi Hospital, Medical School of NingBo University, NingBo, China, [3]Xi'an Jiaotong University, Xi'an, China, [4]Department of Surgery, University of Rochester Medical Center, Rochester, NewYork

Objectives: The purpose of this study was to investigate the role of small interference RNA (siRNA) on expression of E637K-hERG (human ether-a-go-go-related gene) mutant and whether it can be used to rescue the mutant's dominant-negative suppressive effects on hERG protein channel function.
Methods: Western blot was performed to select the most sensitive siRNs to target E637K-hERG mutant knockdown. Confocal laser scanning microscope was performed to monitor cellular localization of wild-type (WT) -hERGandE637K-hERG with or without siRNA. Patch-clamp technique was used to assess the effect of siRNA on the electrophysiologic characteristics of the rapidly activating delayed rectifier K^+ current IKr of the hERG protein channel.
Results: siRNA led to a significant decrease in the level of E637K- hERG protein but did not affect the level of WT-hERG protein. WT-hERG localization in cells coexpressing E637K-hERG mutant was restored to the membrane by siRNA. The siRNA-mediated inhibition of E637K-hERG mutant restored the maximum current and tail current amplitudes. Furthermore, siRNA treatment rescued the kinetic properties of WT/E637K-hERG protein channel to a level comparable to that of WT-hERG protein channel.
Conclusions: Our findings illustrated that siRNA can effectively inhibit E637K-hERG protein expression and rescue the dominant- negative effect of this mutation by restoring the kinetic properties of hERG protein channel. It has potential clinical implications with regard to the possibility of using siRNA in the treatment of LQTS.

GW25-e0603

Expression and distribution characteristics of Nestin-positive cells in the myocardial tissue of mouse

Peng Chaoquan[1], Wu Bingyuan[1], Jiang Meihua[2], Li Guilan[2]
[1]Department of Cardiology, the Third Affiliated Hospital of Sun Yat-Sen University, [2]Center for Stem Cell Biology and Tissue Engineering, Zhongshan School of Medicine, Sun Yat-Sen university

Objectives: The main aim of this study was to systematically evaluate the expression patterns of the Nestin in the developing or damaged adult heart issue, and probe into whether Nestin can be as a marker of cardiac stem cell.
Methods: Nestin expression was assessed in the embryonic 13.5 d and postnatal 1d, 7d, 1M, 3M old Nestin-GFP transgenic mouse heart tissue by fluorescence microscopy, real-time quantitative PCR and RT-PCR. Myocardial infaction model was established by ligation of left anterior descending coronary in adult Nestin-GFP mice and the Nestin expression was observed in the myocardium at 7d after injury. Then, the correlation between Nestin and other stem cell markers' expression in mouse heart tissue were determined by immunofluoresent assay.
Results: In embryonic 13.5 d, the Nestin mainly expressed in the brain, spinal cord and the retina, and also can be observed in the heart tissue. After the mouse was born, Nestin expression is gradually reduced with growth, and that was also confirmed by the RT-PCR, Q-PCR analysis. Nestin-positive cells increased significantly in myocardial infarction area compared to the normal tissue. Sca-1, c-kit, Isl-1 and Nkx2.5 are widely expressed in heart tissue, but not co-expressed with Nestin. However, in normal and injured tissue, Nestin was co-expressed with vimentin and musashi-1, neural cell marker.
Conclusions: These results indicate that nestin expression is highly correlated with cardiac development, and the Nestin-positive myocardial cell might be arise from neural linage cells, which suggest that such cells play an important role in the growth and maintenance of the cardiogenesis and regeneration.

GW25-e0610

A Novel Model of Intimal Hyperplasia in the Bama Miniature Pig

Yao Jianting, Jianting Yao, Ye Tian
The First Affiliated Hospital of Harbin Medical University

Objectives: To develop a bama miniature pig intimal hyperplasia model in superficial femoral artery.
Methods: Following 1 month of a 3% cholesterol diet, 4 pigs underwent surgical perfusion with distilled water (n=8). 3 pigs were subjected to sham-operation for control (n=6). After 3 months of the same diet, sonography and histologic sections of the vessels were analyzed.
Results: Intimal hyperplasia was confirmed in experimental group (8 of 8), whereas the control group remained intact. Lumen area was drastically decreased as assessed by sonography. Histologic sections showed that arteries of experimental group had a increased intimal areas (0.42 ± 0.03 mm^2), increased intimal area/Media area ratios (0.5 ± 0.12 mm^2) and decreased lumen areas (0.35 ± 0.05 mm^2 vs 0.62 ± 0.03 mm^2 $P<0.05$).
Conclusions: This novel intimal hyperplasia model may be a useful tool for evaluating drugs and therapeutic devices.

GW25-e0741

Calreticulin is localized in the mitochondria of rat cardiomyocytes and affected by furazolidone

Shan Hu, Lin Lin, Yan Rui, Zhang Ming, Zhu Yanhe, Wei Jin
Department of Cardiology, The Second Affiliated Hospital, Xi'an Jiaotong University

Objectives: Calreticulin is a calcium-buffering protein which is predominately located in endoplasmic reticulum. We have previously shown calreticulin is also localized in the myocardial mitochondria and up-regulated in a rat model of furazolidone-induced dilated cardiomyopathy. The aim of this study was to determine whether calreticulin is localized in the mitochondria of rat cardiomyocytes and whether mitochondrial calreticulin is affected by furazolidone.
Methods: The mitochondrial preparations were isolated from primary cultured neonatal rat cardiomyocytes and purified by differential centrifugation. The immunoreactivities of calreticulin and markers for cytosol, nucleus, endoplasmic reticulum and plasma membrane were detected by western blot. The distribution of calreticulin to mitochondria was further confirmed by immuno-electron microscopy, flow cytometry and laser scanning confocal microscopy (double staining with MitoTracker Red and calreticulin). To study whether the content of mitochondrial calreticulin was affected by furazolidone, the rat cardiomyocytes were exposed to 100 μmol/L furazolidone for 48 h and then the mitochondrial calreticulin expression was analyzed using western blot.
Results: Western blot and immune-electron microscopy showed that calreticulin was present in the mitochondria of rat cardiomyocytes; moreover, the co-localization of calreticulin and mitochondria was further confirmed by flow cytometry and laser scanning confocal microscopy. Furazolidone treatment significantly increased the content of mitochondrial calreticulin by 3.7 ± 0.7 fold ($P<0.05$) in the rat cardiomyocytes.
Conclusions: In summary, the present results suggest that calreticulin is localized in the mitochondria of rat cardiomyocytes and such localization is affected by furazolidone.

GW25-e0767

Bisphenol A can injure the heart via DNA damage

Yanfei Li, Xucheng Li, Jue Li
Tongji University

Objectives: Bisphenol A (BPA) is a man-made high volume production chemical and human is widely-spread exposure to BPA. Previous studies have showed that the BPA exposure is associated with heart disease, but the mechanisms of BPA on the heart are still unclear. The purpose of this research is to investigate the relation between the concentrations of BPA and severity of the lesions in the heart and analyze the molecular mechanism of BPA harmful effect.
Methods: Mice were subcutaneously injected with normal saline or 0.1, 1 and 10mg/kg/day BPA for 1 month, and then were detected by Vevo 770 ultrasonic diagnostic apparatus, respectively. The cardiomyocytes were isolated from neonatal rats and were treated by PBS or 0.1, 1 and 10uM BPA. The protein of γH2AX was detected by western blot. The mRNA level and the protein level of P21 were tested by real-time PCR and western blot. The protein maps of the cardiomyocytes stimulated by PBS or BPA were measured by two-dimensional gel electrophoresis and the differential protein spots were identified by mass spectrometry.
Results: EF value and FS value were significantly decreased in 1 and 10mg/kg/day BPA groups comparing with normal saline group, and BPA produced a dose-dependent reduction in EF and FS value. The expression of γH2AX and P21 were obviously increased with the concentration of BPA in a dose-dependent manner. Some differentially expressed proteins were determined to be the signal transduction associated proteins of DNA damage.
Conclusions: This study mainly reveals that BPA is harmful to the heart and cardiomyocytes. Its mechanism may be that BPA causes DNA damage in cardiac muscle cell.

GW25-e0775

Hepatocyte Growth Factor Suppresses Hypoxia/Reoxygenation-induced XO Activation in Cardiac Microvascular Endothelial Cells

Zhang Yingqian, Hu Shunying, Chen Yundai
Chinese PLA General Hospital

Objectives: To detect the effect of hepatocyte growth factor (HGF) on xanthine oxidase (XO) under hypoxia/reoxygenation (H/R) conditions in rat cardiac microvascular endothelia cells (CMECs).
Methods: Primary cultured rat cardiac microvascular endothelia cells (CMECs) were exposed to 4h of hypoxia and followed by 1h of reoxygenation. Generation of ROS and cytosolic Ca^{2+} concentration was measured by flow cytometry qualification of DCFH-DA and fluo-3 AM staining cells, respectively. XDH mRNA was qualified by RT-PCR analysis. XO activity was determined by colorimetric assay and XO protein levels were determined by Western blot.
Results: After hypoxia/reoxygenation (H/R), cellular ROS production significantly increased. Both XO activity and XO protein increased after H/R. Cellular ROS elevation were inhibited by allopurinol (a potent XO inhibitor), indicting XO accounting for the generation of ROS after H/R. In addition, XDH mRNA increased after H/R, indicating a de novo XDH synthesize, which need to be converted to XO to become a source of superoxide. Pretreatment of HGF inhibited the elevation of XO activity and XO protein level after H/R; however, HGF has no effect on the increase of XDH mRNA. It has been reported that Ca^{2+} acts in regulating the post-transcripitional conversion from XDH to XO, and we also find an increase of the cytosolic Ca^{2+} in CMECs after H/R. BAPTA-AM, a cell-permeable Ca2+ chelator, prevented the increase of XO activity and XO protein levels, implicating the elevated cytosolic Ca^{2+} concentration involvement in XO conversion and XO activation. Furthermore, HGF inhibited the elevation of cytosolic Ca^{2+} concentration in CMECs after H/R. Thus, HGF inhibited XO activation and XO protein production after H/R by blocking the elevation of cytosolic Ca^{2+} concentration in CMECs.
Conclusions: These findings suggest a novel mechanism whereby HGF inhibited XO-generated ROS production after H/R treatment. H/R induces a de novo synthesize of XDH, the XO precursor. In addition, H/R increases cytosolic Ca^{2+} concentration and promotes a Ca^{2+} -involved XO conversion and XO activation. HGF has no effect on the increase of XDH mRNA; however HGF inhibited the elevation of XO protein level and XO activity after H/R in the post-transcriptional level primarily by inhibiting the increase of cytosolic Ca^{2+} concentration.

GW25-e0784

Knock-down of metallothionein exacerbates intermittent hypoxia induced oxidative and inflammatory injury in aorta

Zhou Shanshan, Yin Xia, Zhang Zhiguo, Zheng Yang
The Center of Cardiovascular Diseases at the First Hospital of Jilin University

Objectives: Obstructive sleep apnea (OSA) is an independent risk factor for cardiovascular diseases possibly via intermittent hypoxia (IH) - elicited oxidative stress and inflammation, while metallothionein (MT) has been recognized as an inducible antioxidant which may protect against damages from a variety of oxidative stimuli. The present study was to explore the effect of MT on IH-induced aortic pathogenic changes.
Methods: To mimic hypoxia/reoxygenation events that occur in adult OSA patients, mice were exposed to IH for up to 8 weeks. The IH paradigm consisted of alternating cycles of 20.9% O_2 /8% O_2 F_IO_2 (30 episodes per hour) with 20 seconds at the nadir F_IO_2 for 12 hours a day during the light phase. Markers of oxidative damages, inflammation, and vascular remodeling were observed by immunohistochemical staining after 3 days, 1, 3 and 8 weeks after IH exposures.
Results: Endogenous MT was induced after 3 days of IH, but was significantly decreased after 8 weeks of IH. Compared with the wild-type mice, MT knock-out mice exhibited earlier and more severe pathogenic changes of oxidative damages, inflammatory responses and cellular apoptosis, as indicated by the significant